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CERTAIN TRACE ELEMENTS IN EXPERIMENTAL MYOCARDIAL INFARCTION AGAINST A BACKGROUND OF HYPERTENSION AND ATHEROSCLEROSIS

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CERTAIN TRACE ELEMENTS IN EXPERIMENTAL MYOCARDIAL INFARCTION AGAINST A BACKGROUND OF HYPERTENSION AND ATHEROSCLEROSIS

(Nekotorye mikroelementy pri eksperimental'nom infarkte miokarda pri nalichii gipertonii i ateroskleroza)

A. V. Aronova

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CERTAIN TRACE ELEMENTS IN EXPERIMENTAL MYOCARDIAL INFARCTION AGAINST A BACKGROUND OF HYPERTENSION AND ATHEROSCLEROSIS

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Among the various kinds of metabolic disorders during myocardial infarction, an important role is played by pathology of trace element metabolism. This is due to the fact that trace elements, interacting with enzymes, vitamins and hormones, participate in the oxidation-reduction processes, changes in which are very important in the formation and course of myocardial infarction. During myocardial infarction, therefore, there is a disturbance of energy processes, processes of oxidizing phosphorylation, in which participate ions of manganese, zinc, iron, etc. [20] Changes in the ratio of these ions can ultimately lead to a change in contractile functions of the cardiac muscle. [7] Ions of copper and manganese take part in the oxidation of catecholamines, whose role in the pathogenesis of myocardial infarction is well known. [2, 15, 16]

A number of studies reveal regular shifts in the content of trace elements in the blood and tissues during myocardial infarction. [3, 5, 7, 11, 12, 18, 19, 21] On the basis of data concerning the known effect of prior hypertension and atherosclerosis on the course of myocardial infarction, as well as the frequent combination of these ailments, we studied the question of how the combination of these kinds of pathology affect changes in the content of trace elements in cases of myocardial infarction.

Material and methods

Tests were made on two series of rabbits with observations of 5-6 months. In series I, the control (10 rabbits) myocardial infarction was reproduced in the intact heart of healthy animals. In series II, the test (11 rabbits) myocardial infarction was induced against a background of prior renal hypertension and cholesterol atherosclerosis. In addition, the trace element level was determined in tissues of 10 healthy rabbits.

Hypertension was induced in animals in the test series by ischemization of the kidneys by step-by-step application of rubber caps to both kidneys. After stabilization of arterial pressure at a high level (171.4±9.0 mm), experimental atherosclerosis was produced by feeding the rabbits 0.3 g of cholesterol per 1 kg weight for 3 months. At the height of development of hyper-

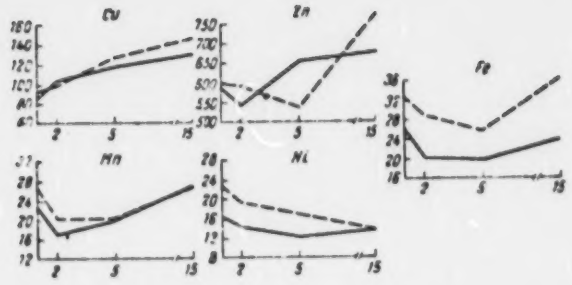

Figure 1. Content of trace elements in the blood of rabbits with myocardial infarction against a background of hypertension and atherosclerosis (solid line) and with myocardial infarction in an intact heart (dashed line).

Horizontally — period of test (in days); vertically — content of trace elements (in μg%).

tension and atherosclerosis, acute coronary occlusion was induced by ligation of the descending branch of the left coronary artery at the boundary between its upper and middle third. Arterial pressure was measured bloodlessly in the common carotid artery, first brought out to the skin according to the method of Van Leersum. The content of copper, zinc, manganese, nickel and iron was determined in whole blood and tissues by the emission spectrum analysis method in an ISP-28 spectrograph. Dynamic studies of the blood were made 2, 5 and 15 days after ligation of the coronary artery. Data obtained during myocardial infarction were compared with initial figures. In rabbits with myocardial infarction against a background of hypertension and atherosclerosis, results obtained the day before the coronary occlusion were used as initial levels. On the 16th day the animals were killed and the content of trace elements determined in the liver as well as in the infarcted section of the myocardium.

Numerical data were statistically analyzed by the difference method. [10]

Results of study

Studies showed that during myocardial infarction there are serious changes in the content of the trace elements in question in whole blood as well as in tissues.

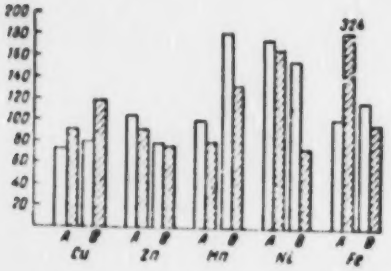

Figure 2. Content of trace elements (% of normal) in the myocardium (A) and liver (B) of rabbits with myocardial infarction against a background of hypertension and atherosclerosis (white columns) and with myocardial infarction in an intact heart (shaded columns).

The content of copper in the blcod of animals in both the test and control series was already reliably increased in the acute period of myocardial infarction and reached the highest level by the 15th day of observation ($P<0.02$; Fig. 1). At the same time, in animals in the control series, the content of copper in the myocardium and liver on the 15th day was slightly reduced, while in rabbits in the test series, the amount of this trace element in the myocardium was close to normal, and in the liver there was a tendency toward its increased concentration in comparison with normal (Fig. 2).

A reliable reduction in the level of manganese was established simultaneously in the blood of rabbits in both series, most pronounced on the 2nd day after ligation of the coronary artery. By the 5th day of myocardial infarction, the amount of manganese in the blood of animals of experimental series began somewhat to increase but still remained lower than the initial amount ($P<0.001$). Only on the 15th day of observation the level of manganese in the blood of animals of the control series became normalized, and somewhat exceeded its initial value ($P>0.05$) in rabbits of experimental group (see Figure 1).

At the same time, the amount of manganese in the myocardium of test rabbits was slightly reduced; in control animals it did not differ from normal. An accumulation of manganese was observed in the liver of animals in both series (see Fig. 2).

The level of nickel in the blood of rabbits in both series was reduced on all days of observation, the greatest reduction being noted in the blood of animals in the control series on the 15th day of observation. At the same time, in the myocardium of rabbits in both series, as well as in the liver of control animals, a significant increase was observed in the nickel content. In contradiction to these data, in rabbits with myocardial infarction against a background of hypertension and atherosclerosis, the level of nickel in the liver was reduced ($P<0.05$; see Fig. 2).

With regard to the zinc content, we found a tendency toward its reduction in the blood of rabbits in both series during the acute period of infarction with subsequent increase on the 15th day (see Fig. 1). In cardiac muscle the concentration of zinc did not differ markedly from normal, while in the liver a very slight reduction in its level was observed (see Fig. 2).

The level of iron in the blood of animals in both series was reliably reduced in the acute period of myocardial infarction. By the 15th day in rabbits in the control series, the iron content slightly exceeded the initial

value ($P>0.05$); initial levels were not reached in animals in the test series (see Fig. 1). In the cardiac muscle of rabbits with myocardial infarction against a background of hypertension and atherosclerosis, by the 15th day a pronounced (over 3 times) increase was noted in the iron content; while in control animals the iron content was within normal limits. There was a slight increase in the iron content in the liver of animals in the control series ($P>0.05$); in test rabbits, the content of iron in the liver did not differ from normal.

Discussion

In experimental myocardial infarction during the acute period, therefore, a reduction was recorded in the content of manganese, nickel, zinc and iron and an increase in the level of copper in the blood. These changes are connected with the redistribution of trace elements among the organs and the blood and reflect the general complex reaction of the body to a "stress" situation. Evidently, during this period there is a migration of trace elements from the depot and blood to the cardiac muscle; this is also confirmed by literature data.[3, 6, 9] The increased copper content in the blood, which is already evident in the acute period, is connected with the stimulation of pain and endocrine shifts, as well as with stimulation of the sympatico-adrenal system, resulting in increased excretion to the blood of catecholamines, whose oxidizer is the copper-containing protein — ceruloplasmin. [2-4, 13, 14]

By the start of the scarring processes in the focus of necrosis (15th day), there is a tendency toward an increase in the level of all tested trace elements in the blood except nickel (see Fig. 1). This is evidently connected with the appearance in the blood of ions and enzymes and with shifts in the ratio of protein components of the blood as the result of the resolution of necrotic masses. We must note that changes in the level of trace elements in organs, reflecting the redistributive reaction (reduction in the amount of copper and increase in the nickel content in the myocardium and liver of control animals, reduction in the level of zinc in the liver and manganese in the myocardium, etc.), are typical in general of animals in the control series. In test rabbits, changes in the content of trace elements in organs reflect more serious metabolic disturbances caused by prior hypertension and atherosclerosis. Thus, in animals in the test series, on the 16th day a significant accumulation of iron was found in the cardiac muscle, while in control rabbits its content was within normal limits; a reduction in the level of nickel was noted in the liver while in control rabbits it was increased. The reduced level of copper in the myocardium and liver, found in animals in the control series, was not noted in test rabbits.

As iron is deposited in increased amounts in the inflammatory or necrotic focus [6, 9] and accelerates healing processes in the focus of necrosis [1], it becomes understandable that its deposition increases in the myocardium, appearing on the 16th day in animals in the test series, in which the course

of the infarction was more severe and scarring processes had not concluded by this time.

The lack of any reduction in the level of copper in the myocardium and a tendency toward its slight increase in the liver of test animals could, evidently, be due to the accumulation of the trace element in these organs during atherosclerosis.[8, 17]

The accumulation of manganese in the liver of animals in both series by the start of scarring processes in the cardiac muscle can be connected with activation of oxidizing processes there, as it is known that manganese is a cofactor of oxidizing phosphorylation. This could serve as a favorable prognostic sign, as to some degree it indicates the activation of regeneration processes.

Conclusions

1. In the acute period of myocardial infarction against a background of hypertension and atherosclerosis,a reduction is noted in the content of zinc, manganese, nickel and iron and an increase in the level of copper in the blood.

2. By the start of scarring processes in the myocardium,the content of zinc, manganese and iron in the blood is close to the initial level, the amount of nickel remains reduced, the level of copper continues to remain high. At this period in the cardiac muscle there is a significant accumulation of iron, an increase in the nickel content, a slight increase in the level of manganese; the content of copper and zinc is within normal limits. In the liver the level of nickel and zinc is reduced, manganese is increased, zinc and iron are within normal limits.

3. The direction of changes in the content of trace elements in the blood in cases of myocardial infarction against a background of hypertension and atherosclerosis is the same as with infarction in an intact heart. However, the more severe shifts in the content of trace elements in organs of animals in the test series indicate that prior hypertension and atherosclerosis aggravate disorders of the metabolism of trace elements during myocardial infarction.

REFERENCES

1. Altukhova, D.M. In the book: Materialy 6-go Vsesoyuzn. soveshchaniya "Mikroelementy v sel'skom khozyaystve i meditsine" (Materials of the 6th All-union conference"Trace elements in agriculture and medicine") Kiev, 1963, p. 621.

2. Anshelevich, Yu.V. Ter. arkh., No. 7, 1963, p. 60.

3. Bala, Yu.M., V.V. Ryabova and G.I. Furmenko. Ter. arkh., No. 4, 1969, p. 87.

4. Voynar, A.O., V. R. Soroka and Ye.V. Sabadash. In the book: Materialy Vsesoyuzn. simpoziuma "Mikroelementy i nervnaya sistema" (Materials of the All-union symposium "Trace elements and the nervous system") Baku, 1966, p. 6.

5. Dovgyallo, T.Kh. and V.T. Tishkovskiy. Ter. arkh., No. 4, 1970, p. 84.

6. Kasab'yan, S.S. Probl. tub., No. 2, 1961, p. 91.

7. Kneta, Z.Ya. In the book: Materialy 3-y konferentsii patologoanatomov Latvii (Materials of the 3rd conference of pathologo-anatomists of Latvia). Riga, 1964, p. 386.

8. Lemzyakova, T.G. In the book: Mikroelementy v meditsine" (Trace elements in medicine), Kiev, No. 1, 1968, p. 131.

9. Neyelov, B.G. In the book: Materialy nauchnoy konferentsii "Morfologiya, fiziologiya i patologiya serdtsa, sosudov i krovi" (Materials of the scientific conference "Morphology, physiology and pathology of the heart,vessels and blood"). Leningrad, 1967, p. 46.

10. Oyvin, I.A. Pat. fiziol., No. 4, 1960, p. 76.

11. Rafalovich, M.B., and G.T. Tarala. Ter. arkh., No. 4, 1970, p. 76.

12. Rachinskiy, I.D. Zaravookhr. Kazakhstana, No. 12, 1968, p. 40.

13. Ryabova, V.V. Mikroelementy krovi i tkaney pri eksperimental'nom infarkte miokarda (Trace elements in the blood and tissues during experimental myocardial infarction). Author's abstract of candidate's dissertation. Voronezh, 1968.

14. Sakfel'd, E.A. and G.A. Babenko. Nauchn. zapiski Stanislavsk. med. in-ta, No. 3, 1959, p. 185.

15. Furkalo, N.K. Kardiologiya, No. 7, 1967, p. 77.

16. Furmenko, G.I. Nekotorye mikroelementy pri ateroskleroze i infarkte miokarda (Several trace elements in atherosclerosis and myocardial infarction). Candidate's dissertation. Voronezh, 1968.

17. Shalayev, F.T. In the book: "Mikroelementy v sel'skom khozyaystve i meditsine" (Trace elements in agriculture and medicine). Ulhan-Ude, 1966, p. 22.

18. D'Alonzo, C and S. Pell. Arch. environm. Health, Vol. 6, 1963, p. 381.

19. Hegte, B., G. Griffith and E. Butt. Proc. Soc. Exp. Biol. (N.Y.), Vol. 107, 1961, p. 734.

20. Lindberg, O and L. Ernster. Nature, Vol. 173, 1954, p. 1038.

21. Wester,P. Acta Med. Scand., Vol. 178, 1965, p. 765.